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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,525	07/09/2001	Jay M. Short	DIVER1230-2	7453

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	17

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/902,525	SHORT ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23,40,41,67-85 and 93-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,40,41,67-85 and 93-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants amendment of the specification, cancellation of claims 24-39, 42-66 and 86-92 and the amendment of claims 1-23, 40, 41, 67-85 and the addition of new claims 93-108, Paper No. 13, 7/28/2003, is acknowledged. Claims 1-23, 40, 41, 67-85 and 93-108 are still at issue and are present for examination.

Applicants' arguments filed on 7/28/2003, Paper No. 13, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-5, 67-81, 82, 83, 84 and 93-108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 67-81, 82, 83 and 84 remain indefinite in the recitation of the terms "high, moderate and low stringency" as the specification does not define what conditions constitute "stringent". While page 13 and 40 of the specification describe some conditions which are encompassed by various hybridization stringencies, there is nothing to suggest that other conditions would not also be included within the scope of these terms and in the art what is considered high, moderate and low stringency varies

widely depending on the individual situation as well as the person making the determination. As such it is unclear how homologous to the sequence of the referred to nucleic acid, a sequence must be to be included within the scope of these claims.

In response to the above rejection which was originally made for claims 3-5, 67-81, 82, 83 and 84, applicants amended claims 3-5, however applicants have not amended claims 67-81, 82, 83 and 84 and applicants have not commented as to these claims.

Claims 3-5 and 93-108 are indefinite in that the newly added hybridization conditions meant to clarify "high", medium" and "low" stringency are unclear. These amended claims are unclear with respect to two different issues. First, claims 3-5 are indefinite in the newly added recitations referring to the conditions that applicants intend to define high, medium and low stringency, that states "...that **include** a wash under conditions including..." Specifically it is unclear if applicants are intending for each of the recited stringency conditions, (i.e. high, medium and low) to be defined by the recited conditions or if the recited conditions are but one of many potentially different conditions **included** in the recited stringency conditions.

Claim 3 (claims 93-108 dependent on) is further indefinite in that the recitation "between the hybridization temperature and 68°C, wherein hybridization is carried out at a temperature of between 15°C to 25°C below the Tm." The reference to the hybridization temperature and hybridization being carried out at a temperature of between 15°C to 25°C below the Tm is unclear. Since the Tm is determined by a

specific duplex of nucleic acids it is not clear how one can define such a Tm, a number that is being used to define a set of encompassed nucleic acids, by those nucleic acids encompassed by the set. In essence it appears that applicants are presenting a "circular limitation" on the claim, because applicants are defining the encompassed nucleic acids by a Tm, wherein the Tm is defined by the nucleic acids.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-5, 6-14, 16-21, 22, 23, 41, 67-81, 82-85 and 93-108 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action as it applied to previous claims 3-5, 6-14, 15, 16-21, 22, 23, 40, 41, 67-81, 82-85. Claims 15 and 40 have been removed from the rejection. In response to the rejection applicants have amended claims 3-23, 40, 41, 67-85 and the added new claims 93-108 and traverse the rejection as it applies to the newly amended and added claims.

Applicants submit that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that applicants were in possession of

the claimed invention. In support of applicants position applicants refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. 112 first paragraph, specifically example 14, in which a claim reciting variants is claimed by sequence identity and function (i.e. catalyze the reaction of A to B). Based on this example, applicants suggest that these guidelines recognize that the written description requirement is met for a genus of polypeptides described by structure, a physico-chemical property and a defined function, and thus applicants conclude that the genus of claimed polynucleotides also meet the written description requirements of 112. Applicants argument is not found persuasive because while the rejected claims have structural limitations, they lack any functional limitation and thus applicants conclusions based on the USPTO guidelines and example 14 are without merit.

Applicants further submit that the claims fully comply with the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997) and comment that the instant claims clearly set forth specific structural and physical characteristics of the claimed hydrogenase-encoding nucleic acids. Applicants additionally submit that the claimed genus of polypeptides all must have a serine protease activity and a specific physical characteristic. These arguments are not found persuasive because applicants are again reminded that the rejected claims have no functional limitation and contrary to the presented example 14 of the USPTO Guidelines the rejected claims have minor structural limitations (i.e. hybridization or sequence identity to a mere 20 residues of SEQ ID NO: 21, a 765 nucleic acid sequence).

Applicants are reminded that hybridization to a nucleic acid which encodes a polypeptide that has phosphatase activity does not necessitate that the claimed nucleic acid encodes a polypeptide with phosphatase activity, nor does the function of the polypeptide encoded by the nucleic acid, which the claimed nucleic acid hybridizes to, satisfy the description requirement for the claimed nucleic acid.

Applicants finally refer to claims from a number of issued U.S Patents suggest that claims directed to nucleic acids defined by sequence identity and function have been issuing for years. Applicants also state that these are included as Exhibit A, however the referred to claims could not be found as Exhibit A. Regardless, the issuing of claims directed to polypeptides defined by sequence identity and function is acknowledged, however, as discussed repeatedly above the currently rejected claims have no such limitations and thus remain rejected.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-5, 6-14, 15, 16, 17-21, 22, 23, 40, 41, 67-81, 82-85 and 93-108 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide having phosphatase activity, wherein said polypeptide comprises SEQ ID NO: 30, does not reasonably provide enablement for any nucleic acid or polynucleotide probe which is fully complementary to a portion of SEQ ID NO: 21. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action as it applied to previous claims 3-5, 6-14, 15, 16-21, 22, 23, 40, 41, 67-81, 82-85. In response to the rejection applicants have amended claims 3-23, 40, 41, 67-85 and the added new claims 93-108 and traverse the rejection as it applies to the newly amended and added claims.

Applicants maintain that the specification enabled the skilled artisan at the time of the invention to identify and make and use a genus of phosphatases to practice the claimed methods. Applicants assert that the state of the art at the time of invention and the level of skill of the person of ordinary skill was very high, such that it would not have taken undue experimentation to make and use the claimed invention including identification of nucleic acids encoding phosphatases. Applicants argument is not found persuasive with respect to claims 3-5, 6-14, 16-21, 22, 23, 41, 67-81, 82-85 and 93-108 or the same reasons as discussed above, the rejected claims are not limited to nucleic acids which encode phosphatases, and thus any argument based on such a limitation is flawed.

With respect to those claims which are directed to nucleic acids that indeed encode a phosphatase or methods of expressing said nucleic acid, claims 1, 2, 15 and 40, applicants are reminded that the claimed genus is considerably large (i.e. those nucleic acids which are merely 50% identical to SEQ ID NO: 21) and thus the necessary teachings and guidance to make a majority of those nucleic acids encompassed by the claims must be quite high. With respect to such an argument

applicants submit that whether large numbers of compositions must be screened is irrelevant to an enablement inquiry. Applicants argument is not found persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a phosphatase) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated, the specification does not support the broad scope of the claims which encompass any nucleic acid or probe has merely 50% sequence identity to SEQ ID NO: 21, because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without its functional activity; (B) the general tolerance of the claimed polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of the polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation

that would be required to determine which substitutions would be acceptable to retain functional/biological activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those nucleic acids of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of modifications of any nucleic acid encoding any phosphatase, wherein said nucleic acid has a mere 50% sequence identity to SEQ ID NO: 21. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The rejection of claims 4, 5, 6-14, 15, 16, 17-21, 67-70, 79 and 85 under 35 U.S.C. 102(e) as being anticipated by Hirschberg et al. (U.S. Patent No: 5,792,903) is withdrawn in light of applicants amendment of claims 4, 5, 6-14, 15, 16, 17-21, and because the nucleic acid taught by Hirschberg et al. would not hybridize to the target region to form a detectable target:probe duplex.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
10/28/2003